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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,841	11/23/2005	Peter Franz Ertl	PG5024	7352

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EXAMINER

KINSEY, NICOLE

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 10/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/533,841

Applicant(s)

ERTL, PETER FRANZ

Examiner

Nicole E. Kinsey, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 July 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28, 31-33 and 35 is/are pending in the application.
- 4a) Of the above claim(s) 21-23, 28 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20, 24-27, 32 and 35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 5/4/2005.

- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I (claims 1-20) in the reply filed on 7/17/2006 is acknowledged. The traversal is on the ground(s) that Group I and Group IV each contain claims directed to polynucleotides. Applicant's arguments have been found persuasive.

The polynucleotides of Groups I and IV as well as the pharmaceutical composition comprising the vectors are not patentably distinct. Therefore, upon further consideration, claims 24-27, 32-33 and 35 will be rejoined with Group I.

Status of the claims

Claims 1-28, 31-33 and 35 are pending, and claims 21-23, 28 and 31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b). Claims 1-20, 24-27, 32 and 35 are under examination.

Information Disclosure Statement

The information disclosure statement filed 5/4/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Applicant should provide a copy of the references, which have been lined through on the enclosed Form PTO-1449.

Specification

The disclosure is objected to for not containing a brief description of the drawings section. According to 37 CFR 1.74, when there are drawings, there shall be a brief description of the several views of the drawings and the detailed description of the invention shall refer to the different views by specifying the numbers of the figures, and to the different parts by use of reference letters or numerals (preferably the latter).

Appropriate correction is required.

Trademarks

The use of the trademark MPL has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-9, 14 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5, 8, 9 and 14 recite fusion proteins as A-B-C-D, for example. It is not clear if this is meant to denote the arrangement of the sequences in the 5' to 3' direction.

Claims 6 and 7 recite that gp120 sequences are "linked" to other HIV sequences. It is unclear if "linked" means the sequences are directly linked or if the sequences are in the same construct with spacers indirectly linking the sequences.

Claim 8 is drawn to a polynucleotide encoding a gp120-Nef-Tat fusion protein. It is not clear how this protein can result from following the recitations of claims 6 and 7, from which claim 8 depends. The fusion protein of claim 6 is either gp120-Nef or Nef-gp120. Claim 7, which is dependent upon claim 6, is drawn to a polynucleotide encoding a fusion protein where the gp120 sequence of the gp120/Nef containing fusion protein of claim 6 is further linked to a sequence encoding HIV Tat. Again, the protein of claim 6 is either gp120-Nef or Nef-gp120. If the gp120 sequence of either of these proteins is further linked to Tat as recited in claim 7, then one should obtain Tat-gp120-Nef or Nef-gp120-Tat, not gp120-Nef-Tat as recited in claim 8.

Claim 16 is drawn to a polynucleotide where a 5' untranslated region between the promoter and the coding sequence comprises exon 1. It is unclear how an untranslated region can code for an exon. If applicants meant to state "wherein a 5' untranslated region including exon1 of the HCMV IE gene is between the HCMV IE promoter and the coding sequences," then the claim should be amended for clarity.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 11, 13, 17, 18, 24-27 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Nabel et al. (WO 02/32943) as evidenced by Fynan et al.

Nabel et al. discloses double-stranded DNA vectors comprising sequences that encode an HIV Env (gp120) fused to Nef (pages 58-59) where the env sequences are codon optimized for expression in human cells (page 16, line 30 and pages 58-59). Nabel et al. further teaches the use of non-glycosylated HIV envelope (pages 43-47). Compositions comprising the vectors can be in aqueous solution (page 25, lines 3-6), mixed with a pharmaceutically acceptable adjuvant (page 27, lines 1-15), enclosed in liposome carriers (i.e., particle carriers) (page 25, lines 9-15), and can be used in a prime-boost regimen (page 27, lines 26-27). In addition, Nabel et al. teaches that the compositions can be administered intramuscularly, intraperitoneally, intradermally, subcutaneously, etc. via intradermal delivery devices such as syringes, needleless injection devices, or microprojectile bombardment gene guns (page 33, lines 5-13). It is well known in the art that gold beads are used as carriers for DNA vaccinations via gene guns or microprojectile bombardment as evidenced by Fynan et al.

Claims 1-3, 10, 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Buck et al.

Buck et al. discloses double-stranded DNA vectors comprising sequences that encode an HIV Env-Gag fusion protein.

Claim 32 is rejected under 35 U.S.C. 102(b) as being anticipated by Salfeld et al.

Salfeld et al. discloses a double-stranded DNA vector comprising a functional tat protein fused to two HIV antigens (env and rev).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Catchpole et al. (WO 02/36792).

Claims 15 and 16 are drawn to the polynucleotides of the invention linked to the HCMV IE gene promoter and also the 5' untranslated region of the HCMV IE promoter including exon 1 of the HCMV IE gene.

The teachings of Nabel et al. are outlined above under 35 U.S.C. 102(b). Nabel et al. does disclose the use of the CMV promoter (page 31, lines 31-32), but not the use

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of the HCMV IE gene promoter or the 5' untranslated region of the HCMV IE promoter including exon 1 of the HCMV IE gene.

Catchpole et al. teaches that the use of the HCMV IE gene promoter to drive gene expression is known (page 1, lines 19-33). Catchpole et al. further states that the 5' untranslated region of the HCMV IE promoter including exon 1 of the HCMV IE gene will result in an enhanced level of expression from the HCMV IE promoter (page 2, line 25 to page 4, line 2). Catchpole et al. also teaches that such promoter sequences are good for the expression of HIV antigens (page 5, line 32 to page 7, line 4).

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Nabel et al. to use the HCMV IE promoter and 5' sequences from HCMV IE in order to express HIV antigens/genes. One would have been motivated to do so, given the suggestion by Nabel et al. to use the CMV promoter generally to express HIV antigens and the suggestion by Catchpole et al. to use the HCMV IE promoter specifically to drive expression of recombinant proteins and to use the 5' untranslated sequences for enhanced expression of antigens. There would have been a reasonable expectation of success, given the fact that it is well known that the CMV promoter is a strong promoter and that the CMV promoter is commonly used to express heterologous proteins/antigens (see Catchpole et al., page 1, lines 19-33), including HIV antigens. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

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Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Farina et al. and Roy et al.

The teachings of Nabel et al. are outlined above under 35 U.S.C. 102(b). Nabel et al. does disclose the use of adenovirus as a vector (page 25, lines 16-35), but not a replication-defective adenovirus or Pan 9, 5, 6, or 7.

Farina et al. teaches the use of replication-defective adenovirus C68 to express genes. C68 is another name for Pan 9 as evidenced by Roy et al.

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Nabel et al. to use the C68 (Pan 9) replication-defective adenovirus of Farina et al. One would have been motivated to do so, given the suggestion by Farina et al. that C68 functions as an excellent vaccine for HIV (see Farina et al. page 11612, last paragraph of the discussion) and that humans rarely have neutralizing antibodies to these viruses. There would have been a reasonable expectation of success, given the fact that it is well known to use replication-defective adenoviruses as vaccine vehicles. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. (WO 02/32943) in view of Botarelli et al.

The teachings of Nabel et al. are outlined above under 35 U.S.C. 102(b). Botarelli et al. teaches that glycosylation residues on gp120 can function as hindering structures that limit antigen recognition by T-lymphocytes (see abstract). The non-

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glycosylated form of HIV gp120 of Botarelli et al. was produced by removing the signal sequence. Botarelli et al. states that “[t]he lack of signal sequence prevents passage through the secretory pathway and addition of carbohydrates.”

It would have been obvious to one of ordinary skill in the art to modify the polynucleotides taught by Nabel et al. to use HIV env sequences lacking a secretory signal sequence to produce non-glycosylated HIV Env. One would have been motivated to do so, given the suggestion by Botarelli et al. that glycosylation residues on gp120 can function as hindering structures that limit antigen recognition by T-lymphocytes. There would have been a reasonable expectation of success, given the fact that it is well known that the removal of the secretory signal sequence bypasses the secretory pathway and the addition of carbohydrates, and that others have successfully produced non-glycosylated proteins by removing the secretory signal sequence (see Botarelli et al.). Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nabel et al. in view of Hone et al. (Abstract), Mooij et al. (2001) and Mooij et al.

The teachings of Nabel et al. are outlined above under 35 U.S.C. 102(b). It is well known in the art the vaccines containing multiple HIV antigens produce broader immune responses than vaccines with a single antigen. In fact, Hone et al. states that “[i]t is likely that effective immunity against HIV in humans will require immunization with multiple HIV antigens.” Mooij et al. states that “strong Th responses to multiple antigens

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are beneficial in facilitating effector responses such as CTL responses and/or neutralizing antibodies capable of effectively controlling or ultimately preventing HIV-1 infection. An effective HIV-1 vaccine candidate should not only contain a combination of immune targets distributed over both regulatory and structural viral antigens, but ideally they should elicit a diverse array of immune effector mechanisms to most effectively limit and even prevent virus replication" (last paragraph of discussion). Mooij et al. (2001) also states that an effective prophylactic HIV-1 vaccine must induce strong and multiple effector immune responses (neutralising antibodies, and CTL activity supported by strong Th1/Th2 helper responses), to preferably multiple conserved epitopes (page 308, right column, first full paragraph).

It would have been obvious to one of ordinary skill in the art to modify the methods taught by Nebel et al. to express other HIV antigen combinations as recited in claim 33 in a DNA vaccine. One would have been motivated to do so given the suggestions by Hone et al. and Mooij et al. that multi-antigen HIV vaccines are more effective. There would have been a reasonable expectation of success, given the knowledge that HIV antigens, such as tat, nef, gag, gp120/env, rt, vif, vpu, vpr, etc., are well known in the art, and also given the knowledge that many others have used these antigens, singly or in combination, to produce immune responses *in vivo*. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-20, 24-27 and 35 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18, 20-24, and 28-31 of copending Application No. 10/533,734. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a recombinant polynucleotide molecule comprising HIV envelope sequences fused to at least one HIV nonstructural protein or capsid protein in a vector with a heterologous promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

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Claims 15, 16 and 25 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 14, 15 and 17-20 of U.S. Patent No. 10/485,048. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a recombinant polynucleotide molecule comprising gp120 sequences and an HIV nonstructural protein (Nef and/or Tat) in a vector with an enhanced HCMV IE1 promoter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nicole E. Kinsey, Ph.D. whose telephone number is (571) 272-9943. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nicole E Kinsey, Ph.D.
Examiner
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A handwritten signature in black ink, appearing to read "Bruce Campell". The signature is fluid and cursive, with the first name "Bruce" and last name "Campell" clearly distinguishable.

BRUCE R. CAMPPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600